(FILE 'HOME' ENTERED AT 10:39:03 ON 03 JUN 1998)

FILE 'GENBANK' ENTERED AT 10:39:12 ON 03 JUN 1998

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            E GODOWSKI/AU
L1        110 S E4 OR E5
L2          0 S L1 AND TIE?
L3          0 S L1 AND NL1
L4          0 S L1 AND TIE2
L5          0 S L1 AND (FETAL LUNG)
L6          0 S L1 AND GGCTGAGGGG?
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US PAT NO: 5,506,107 [IMAGE AVAILABLE] L1: 12 of 47
DATE ISSUED: Apr. 9, 1996
TITLE: Selecting ligand agonists and antagonists
INVENTOR: Brian C. Cunningham, Piedmont, CA
Abraham M. DeVos, Oakland, CA
Michael G. Mulkerrin, Redwood City, CA
Mark Ultsch, Mill Valley, CA
James A. Wells, Burlingame, CA
ASSIGNEE: Genentech, Inc., South San Francisco, CA (U.S. corp.)
APPL-NO: 08/122,548
DATE FILED: Sep. 29, 1993
ART-UNIT: 182
PRIM-EXMR: David Saunders
LEGAL-REP: Laura Terlizzi, Emily M. Haliday

US PAT NO: 5,506,107 [IMAGE AVAILABLE] L1: 12 of 47

ABSTRACT:

We have discovered that growth hormones form ternary complexes with their receptors in which site 1 on the hormone first binds to one molecule of receptor and then hormone site 2 then binds to another molecule of receptor, thereby producing a 1:2 complex. We believe this phenomenon is shared by other ligands having similar conformational structure. Assays based on this phenomenon are useful for identifying ligand agonists and antagonists. Sites 1 and 2 are structurally identified to facilitate generation of amino acid sequence variants of ternary complex-forming ligands. Novel variants of growth hormone, prolactin placental lactogen and other related ligands are provided. As a result of our studies with the ternary complex we have determined that selected antibodies to the receptor for these ligands are capable of acting as ligand agonists or antagonists. Novel growth hormones and novel uses for anti-growth hormone receptor antibodies are described.

US PAT NO: 5,521,073 [IMAGE AVAILABLE] L1: 11 of 47
DATE ISSUED: May 28, 1996
TITLE: **TIE**-2 **ligand**, and method of making
INVENTOR: Samuel Davis, New York, NY
Thomas H. Aldrich, Ossining, NY
George D. Yancopoulos, Yorktown Heights, NY
ASSIGNEE: Regeneron Pharmaceuticals, Inc., Tarrytown, NY (U.S. corp.)
APPL-NO: 08/330,261
DATE FILED: Oct. 27, 1994
ART-UNIT: 182
PRIM-EXMR: Garnette D. Draper
ASST-EXMR: Prema Mertz
LEGAL-REP: Robert J. Cobert

US PAT NO: 5,521,073 [IMAGE AVAILABLE] L1: 11 of 47

ABSTRACT:
The present invention provides for an isolated nucleic acid molecule encoding human **TIE**-2 **ligand**. In addition, the invention provides for a receptor body which specifically binds human **TIE**-2 **ligand**. The invention also provides an antibody which specifically binds human

TIE-2 **ligand**. The invention further provides for therapeutic compositions as well as a method of blocking blood vessel growth, a method of promoting neovascularization and a method of promoting the growth or differentiation of a cell expressing the **TIE**-2 **receptor**.

US PAT NO: 5,643,755 [IMAGE AVAILABLE] L1: 8 of 47
DATE ISSUED: Jul. 1, 1997
TITLE: Nucleic acid encoding **tie**-2 **ligand**
INVENTOR: Samuel Davis, New York, NY
Thomas Aldrich, Ossining, NY
George D. Yancopoulos, Yorktown Heights, NY
ASSIGNEE: Regeneron Pharmaceuticals Inc., Tarrytown, NY (U.S. corp.)
APPL-NO: 08/319,932
DATE FILED: Oct. 7, 1994
ART-UNIT: 182
PRIM-EXMR: John Ulm
ASST-EXMR: Prema Mertz
LEGAL-REP: Gail M. Kempler, Robert J. Cobert

US PAT NO: 5,643,755 [IMAGE AVAILABLE] L1: 8 of 47

ABSTRACT:
The present invention provides for **TIE**-2 **ligand** substantially free of other proteins. The invention also provides for an isolated nucleic acid molecule encoding **TIE**-2 **ligand**. In addition, the invention provides for a receptor body which specifically binds **TIE**-2 **ligand**. The invention also provides an antibody which specifically binds **TIE**-2 **ligand**. The invention further provides for therapeutic compositions as well as a method of blocking blood vessel growth, a method of promoting neovascularization and a method of promoting the growth or differentiation of a cell expressing the **TIE**-2 **receptor**.

US PAT NO: 5,650,490 [IMAGE AVAILABLE] L1: 6 of 47
DATE ISSUED: Jul. 22, 1997
TITLE: **Tie**-2 **ligand** 2
INVENTOR: Samuel Davis, New York, NY
Pamela F. Jones, Fairfield, CT
George D. Yancopoulos, Yorktown Heights, NY
ASSIGNEE: Regeneron Pharmaceuticals, Inc., Tarrytown, NY (U.S. corp.)
APPL-NO: 08/373,579
DATE FILED: Jan. 17, 1995
ART-UNIT: 182
PRIM-EXMR: John Ulm
ASST-EXMR: Prema Mertz
LEGAL-REP: Robert J. Cobert

US PAT NO: 5,650,490 [IMAGE AVAILABLE] L1: 6 of 47

ABSTRACT:
The present invention provides for an isolated nucleic acid molecule encoding human **TIE**-2 **ligand**. In addition, the invention provides for a receptor body which specifically binds human **TIE**-2 **ligand**. The invention also provides an antibody which specifically binds human **TIE**-2 **ligand**. The invention further provides for therapeutic compositions as well as a method of blocking blood vessel growth, a method of promoting neovascularization and a method of promoting the growth or differentiation of a cell expressing the **TIE**-2 **receptor**.

US PAT NO: 5,681,7[illegible] [IMAGE AVAILABLE]
DATE ISSUED: Oct. 28[illegible]997
TITLE: Nucleic acid encoding tek receptor tyrosine kinase
INVENTOR: Martin L. Breitman, deceased, late of Willowdale, Canada, by Jo-Ann Breitman, Executor
Janet Rossant, Toronto, Canada
Daniel J. Dumont, Oakville, Canada
Terry P. Yamaguchi, Toronto, Canada
ASSIGNEE: Mount Sinai Hospital Corporation, Toronto, Canada (foreign corp.)
APPL-NO: 08/278,089
DATE FILED: Jul. 20, 1994
ART-UNIT: 182
PRIM-EXMR: Stephen Walsh
ASST-EXMR: Sally P. Teng
LEGAL-REP: Bereskin & Parr

US PAT NO: 5,681,714 [IMAGE AVAILABLE] L1: 4 of 47

ABSTRACT:
Novel receptor tyrosine kinase protein and isoforms thereof which are expressed in cells of the endothelial lineage, and DNA segments encoding the novel protein and isoforms thereof are disclosed. Methods for identifying ligands which are capable of binding to the receptor protein and methods for screening for agonist or antagonist substances of the interaction of the protein and a ligand are also disclosed.

1. 5,709,858, Jan. 20, 1998, Antibodies specific for Rse receptor protein tyrosine kinase; **Paul J. Godowski**, et al., 424/143.1, 139.1; 435/7.4; 530/387.3, 387.9, 388.22, 391.1, 391.3 [IMAGE AVAILABLE]

2. 5,696,086, Dec. 9, 1997, Methods and kits using macrophage stimulating protein; Hava Karsenty Avraham, et al., 514/12; 530/351, 380 [IMAGE AVAILABLE]

3. 5,684,136, Nov. 4, 1997, Chimeric hepatocyte growth factor (HGF) ligand variants; **Paul J. Godowski**, 530/399, 387.3 [IMAGE AVAILABLE]

4. 5,580,963, Dec. 3, 1996, Single-chain hepatocyte growth factor variants; **Paul J. Godowski**, et al., 530/399 [IMAGE AVAILABLE]

5. 5,547,856, Aug. 20, 1996, Hepatocyte growth factor variants; **Paul J. Godowski**, et al., 435/69.4, 320.1, 325; 530/399; 536/23.51 [IMAGE AVAILABLE]

6. 5,328,837, Jul. 12, 1994, Hepatocyte growth factor protease domain variants; **Paul J. Godowski**, et al., 435/69.4; 530/399; 536/23.51 [IMAGE AVAILABLE]

7. 5,316,921, May 31, 1994, Single-chain hepatocyte growth factor variants; **Paul J. Godowski**, et al., 435/69.4; 530/399; 536/23.51 [IMAGE AVAILABLE]

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(FILE 'USPAT' ENTERED AT 10:44:55 ON 03 JUN 1998)

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L1          47 S TIE1 OR TIE2 OR (TIE?(3A)(RECEPTOR? OR LIGAND?))
               E GODOWSKI, P/IN
L2           7 S E4
               E GURNEY, A/IN
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